

Abstract

X-ray crystallography can be used to screen compounds that are not known ligands of a target biomolecule for their ability to bind the target biomolecule. The method includes obtaining a crystal of a target biomolecule; exposing the target biomolecule crystal to one or more test samples; and obtaining an X-ray crystal diffraction pattern to determine whether a ligand/receptor complex is formed.

The target is exposed to the test samples by either co-crystallizing a biomolecule in the presence of one or more test samples or soaking the biomolecule crystal in a solution of one or more test samples. In another embodiment, structural information from ligand/receptor complexes are used to design ligands that bind tighter, that bind more specifically, that have better biological activity or that have better safety profile.

A further embodiment of the invention comprises identifying or designing biologically-active moieties by the instant process.

In a further embodiment, a biomolecule crystal having an easily accessible active site is formed by co-crystallizing the biomolecule with a degradable ligand and degrading the ligand.